



# D E C L A R A T I O N

I, Kazuya MINAMISAKA, a national of Japan, c/o Sumitomo Chemical Intellectual Property Service, Limited, 5-33, Kitahama 4-chome, Chuo-ku, Osaka 541-8550, Japan, declare that to the best of my knowledge and belief the attached is a full, true, and faithful translation into English made by me of the of Japanese Patent Application Number 2004-068703.

Signed this 2nd of February, 2009

A handwritten signature in cursive script, reading "Kazuya Minamisaaka", written over a horizontal line.

Kazuya MINAMISAKA

JAPAN PATENT OFFICE

This is to certify that the annexed is a true copy of the following application as filed with this Office.

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[Inventor]

[Address] c/o SUMITOMO CHEMICAL COMPANY, LIMITED,  
Kasugadenaka 3-1-98, Konohana-ku, Osaka-shi, Osaka, Japan

[Name] Koji HAGIYA

[Patent Applicant]

[Identification Number] 000002093

[Name] SUMITOMO CHEMICAL COMPANY, LIMITED

[Agent]

[Identification Number] 100093285

[Patent Attorney]

[Name] Takashi KUBOYAMA

[Telephone Number] 06-6220-3405

[Appointed Agent]

[Identification Number] 100113000

[Patent Attorney]

[Name] Toru NAKAYAMA

[Telephone Number] 06-6220-3405

[Appointed Agent]

[Identification Number] 100119471

[Patent Attorney]

[Name] Masayuki ENOMOTO

[Telephone Number] 06-6220-3405

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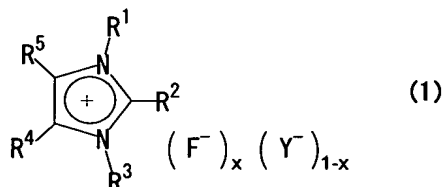
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[Title of Document] SCOPE OF CLAIMS FOR PATENT

[Claim 1]

A method for producing a fluorine-containing compound comprising reacting an organic compound having one or two or more substituents subjected to a nucleophilic substitution fluorination reaction with a mixed alkyl-substituted imidazolium salt containing a fluoride ion represented by the formula (1):

[Formula 1]



wherein R¹ and R³ are the same or different, and each represents an optionally substituted alkyl group, R², R⁴ and R⁵ are the same or different, and each represents a hydrogen atom or an optionally substituted alkyl group, Y⁻ represents a monovalent anion other than a fluoride ion, and 0 < x < 1.

[Claim 2]

The method according to claim 1, wherein the monovalent anion represented by Y⁻ is a halide ion, a borate ion, a phosphate ion, an antimonate ion, a sulfonate ion or an amide ion.

[Claim 3]

The method according to Claim 1, wherein the organic compound having one or two or more substituents subjected to a nucleophilic substitution fluorination reaction is an organic compound wherein one or two or more hydrogen atoms on a saturated hydrocarbon, which may be substituted, are substituted with a substituent subjected to a nucleophilic substitution fluorination reaction.

[Claim 4]

The method according to Claim 1, wherein the organic compound having one or two or more substituents subjected to a nucleophilic substitution fluorination reaction is an organic compound wherein one or two or more hydrogen atoms on an optionally substituted aromatic compound are substituted with a substituent subjected to a nucleophilic substitution fluorination reaction.

[Claim 5]

The method according to Claim 1, wherein the substituent subjected to a nucleophilic substitution fluorination reaction is a chlorine atom, a bromine atom, an iodine atom, a nitro group, a sulfo group, an optionally substituted alkylsulfonyloxy group, an optionally substituted arylsulfonyloxy group, an optionally substituted alkylcarbonyloxy group or an optionally substituted arylcarbonyloxy group.

[Claim 6]

A fluorinating agent represented by the formula (1).

[Title of Document] SPECIFICATION

[Title of the Invention] Fluorinating agent and method for producing a fluorine-containing compound

[Technical Field]

[0001]

The present invention relates to a fluorinating agent and a method for producing a fluorine-containing compound.

[Background Art]

[0002]

Fluorine-containing compounds are very important compounds as various chemical products including pharmaceutical and pesticide compounds and electronic materials, and the intermediates thereof.

[0003]

Various reactions wherein a fluorine atom is introduced to an organic compound using a nucleophilic substitution reaction by a fluorine anion and various fluorinating agents for them have been developed. As methods using potassium fluoride among the fluorinating agent, for example, a method of substituting a chlorine atom on a chlorine-substituted nitrobenzene with a fluorine atom in an aprotic polar solvent (e.g. Non-patent document 1), a method of substituting a chlorine atom or bromine atom on various organic chloride or bromide using potassium fluoride highly activated by a spray dry method (e.g. Non-patent document 2), a method of substituting a sulfonyloxy group of a sulfonic acid ester compound with a fluorine atom using polyethylene glycol 400 as a solvent (e.g. Non-patent document 3), a method of conducting various fluorinations in the presence of an ionic solvent such as an imidazolium salt (e.g. Patent documents 1 and 2) and the like have been known. However, all of these are not enough as industrial methods since a yield and selectivity of

the desired fluorine-containing compound are low, a high temperature or long-time conditions are needed, and a particular apparatus for spray dry is needed.

[0004]

Meanwhile, as methods using a fluorinating agent having a quaternary salt type cation, a method using a quaternary ammonium fluoride (e.g. Non-patent document 4), a method using a quaternary ammonium fluoride in combination with cesium fluoride (e.g. Non-patent document 5) and the like have been known. However, all of them are not enough for industrial methods since a yield and selectivity of the desired fluorine-containing compound are low. Alternatively, as methods using a fluorinating agent having a relatively high fluorinating activity and a quaternary salt type cation, a method using a quaternary ammonium bifluoride (e.g. Non-patent document 6), a method using a quaternary phosphonium bifluoride (e.g. Patent documents 3 and 4) and the like have been known. However, all of them contain highly corrosive and toxic hydrogen fluoride, and hydrofluoric acid is used in the production thereof, and therefore, they are not satisfied industrially.

[0005]

[Patent document 1] WO02/092608 A

[Patent document 2] WO03/076366 A

[Patent document 3] JP 61-161224 A

[Patent document 4] JP 4-124146 A

[Non-patent document 1] J. Amer. Chem. Soc., 78, 6034 (1956)

[Non-patent document 2] Chemistry Lett., 761 (1981)

[Non-patent document 3] Synthesis, 920 (1987)

[Non-patent document 4] J. Org. Chem., 49, 3216 (1984)

[Non-patent document 5] Synthetic Commun., 18, 1661 (1988)



[Non-patent document 6] Tetrahedron Lett., 28, 4733 (1987)

[Disclosure of the Invention]

[Problems to be solved by the Invention]

[0006]

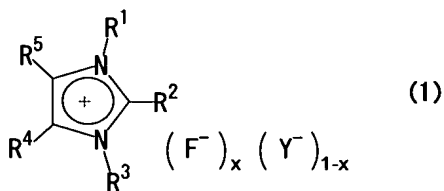
So the present inventor has intensively studied in order to develop an industrially advantageous method for producing a fluorine-containing compound without using a highly corrosive and toxic compound and, as a result, he has found that a nucleophilic substitution fluorination reaction proceed efficiently by using a mixed alkyl-substituted imidazolium of a fluoride ion and the other anion as a fluorinating agent, thereby completing the present invention.

[Means for Solving the Problems]

[0007]

That is, the present invention is to provide a method for producing a fluorine-containing compound comprising reacting an organic compound having one or two or more substituents subjected to a nucleophilic substitution fluorination reaction with a mixed alkyl-substituted imidazolium salt containing a fluoride ion represented by the formula (1):

[Formula 1]



wherein  $R^1$  and  $R^3$  are the same or different, and each represents an optionally substituted alkyl group,  $R^2$ ,  $R^4$  and  $R^5$  are the same or different, and each represents a hydrogen atom or an optionally substituted alkyl group,  $Y^-$  represents a monovalent anion other than

a fluoride ion, and  $0 < x < 1$ .

[Effects of the Invention]

[0008]

According to the present invention, fluorine-containing aliphatic and aromatic compounds can be efficiently produced without using a highly corrosive and toxic compound, and therefore, it is industrially advantageous. Further, since the fluorinating agent of the present invention has also the nature of an ionic liquid in itself, it is easy to recover and reuse thereof. Alternatively, since the fluorinating agent whose melting point is below room temperature can be obtained by selecting  $x$  in the formula (1) accordingly, the reaction using it can be carried out under the wide temperature condition. Therefore, it is also advantageous from the viewpoint of handling industrially and environment.

[Best Mode for Carrying out the Invention]

[0009]

First, the mixed alkyl-substituted imidazolium salt containing a fluoride ion represented by the formula (1) (hereinafter, simply referred to as the fluorinating agent (1)) will be illustrated.

[0010]

In the formula,  $R^1$  and  $R^3$  are the same or different, and each represents an optionally substituted alkyl group, and  $R^2$ ,  $R^4$  and  $R^5$  are the same or different, and each represents a hydrogen atom or an optionally substituted alkyl group.

[0011]

Herein, examples of the alkyl group include a straight chain, branched chain or cyclic C1-20 alkyl group such as a methyl group, an ethyl group, an n-propyl group, an isopropyl group, an n-butyl group, an isobutyl group, a sec-butyl group, a tert-butyl group,

an n-pentyl group, an n-decyl group, a cyclopropyl group, a 2,2-dimethylcyclopropyl group, a cyclopentyl group, a cyclohexyl group and a menthyl group. The alkyl group may be substituted with a C1-20 alkoxy group which may be substituted such as a methoxy group, an ethoxy group, an n-propoxy group, an isopropoxy group, an n-butoxy group, an isobutoxy group, a sec-butoxy group, a tert-butoxy group and a trifluoromethoxy group; a C6-20 aryl group which may be substituted such as a phenyl group, a 4-methylphenyl group and 4-methoxyphenyl group; a C6-20 aryloxy group which may be substituted such as a phenoxy group, a 2-methylphenoxy group, a 4-methylphenoxy group, a 4-methoxyphenoxy group and a 3-phenoxyphenoxy group; a C7-20 aralkyloxy group which may be substituted such as a benzyloxy group, a 4-methylbenzyloxy group, a 4-methoxybenzyloxy group and a 3-phenoxybenzyloxy group; a fluorine atom; a C2-20 alkylcarbonyl group which may be substituted such as an acetyl group and an ethylcarbonyl group; a C7-20 arylcarbonyl group which may be substituted such as a benzoyl group, a 2-methylbenzoyl group, a 4-methylbenzoyl group and a 4-methoxybenzoyl group; a C8-20 aralkylcarbonyl group which may be substituted such as a benzylcarbonyl group, a 4-methylbenzylcarbonyl group and a 4-methoxybenzylcarbonyl group; or a carboxyl group. Examples of the alkyl group substituted with the substituent include a fluoromethyl group, a trifluoromethyl group, a methoxymethyl group, an ethoxymethyl group and a methoxyethyl group, a benzyl group, a 4-fluorobenzyl group, a 4-methylbenzyl group, a phenoxymethyl group, a 2-oxopropyl group, a 2-oxobutyl group, a phenacyl group and a 2-carboxyethyl group.

[0012]

Y<sup>-</sup> represents a monovalent anion other than a fluoride ion.

Examples of the monovalent anion other than a fluoride ion include a halide ion other than a fluoride ion such as a chloride ion, a bromide ion and an iodide ion; a borate ion such as a tetrafluoroborate anion; a phosphate ion such as a hexafluorophosphate anion; an antimonate ion such as hexafluoroantimonate anion; a sulfonate ion such as a trifluoromethanesulfonate anion; and an amide ion such as a bis(trifluoromethylsulfonyl)amide anion.

[0013]

X can be selected at random in the range of  $0 < x < 1$ . When x is close to 0, the productivity as a fluorinating agent goes down and when x is close to 1, the melting point tends to become high. Therefore, a range of about  $0.4 < x < 0.9$  is preferable in order to conduct fluorination efficiently at lower temperature.

[0014]

Examples of the fluorinating agent (1) include a mixed alkyl-substituted imidazolium salt containing a fluoride ion, which consists of a mixed anion of a fluoride ion and a chloride ion and an alkyl-substituted imidazolium cation such as 1,3-dimethylimidazolium cation, 1,2,3-trimethylimidazolium cation, 1,2,3,4-tetramethylimidazolium cation, 1,2,3,4,5-pentamethylimidazolium cation, 1-methyl-3-ethylimidazolium cation, 1,2-dimethyl-3-ethylimidazolium cation, 1,3-diethylimidazolium cation, 1-methyl-3-(n-propyl)imidazolium cation, 1-methyl-3-(n-butyl)imidazolium cation, 1,2-dimethyl-3-(n-butyl)imidazolium cation, 1-methyl-3-(n-pentyl)imidazolium cation, 1-methyl-3-(n-hexyl)imidazolium cation, 1,3-dimethyl-2-ethylimidazolium cation,

1,3-dimethyl-2-(n-propyl)imidazolium cation,  
1,3-dimethyl-2-(n-butyl)imidazolium cation,  
1-dodecyl-2-methyl-3-dodecylimidazolium cation,  
1-ethoxymethyl-3-methylimidazolium cation,  
1-trifluoromethyl-3-methylimidazolium cation and  
1-(n-dodecyl)-2-methyl-3-benzylimidazolium cation, and a mixed  
alkyl-substituted imidazolium salt in which the chloride ions of  
the above-mentioned mixed alkyl-substituted imidazolium salts  
containing a fluoride ion are replaced with bromide ions, iodide  
ions, tetrafluoroborate anions, hexafluorophosphate anions,  
hexafluoroantimonate anions, trifluoromethanesulfonate anions or  
bis(trifluoromethylsulfonyl)amide anions.

[0015]

They may be formed complexes with a compound being inactive  
to a nucleophilic substitution fluorination reaction such as water  
and a polar solvent.

[0016]

The fluorinating agent (1) can be produced using a method  
such as partial salt-exchange reaction of a fluoride such as a silver  
fluoride and potassium fluoride and an alkyl-substituted imidazolium  
salt wherein x is 0 in the formula (1). Alternatively, it may be  
prepared by mixing an alkyl-substituted imidazolium salt wherein  
x is 0 in the formula (1) and an alkyl-substituted imidazolium fluoride  
wherein x is 1.

[0017]

Next, the fluorination reaction of an organic compound having  
one or two or more substituents subjected to a nucleophilic  
substitution fluorination reaction using the fluorinating agent (1)  
will be illustrated.

[0018]

Examples of the organic compound having one or two or more substituents subjected to a nucleophilic substitution fluorination reaction include an organic compound wherein one or two or more hydrogen atoms on a saturated hydrocarbon, which may be substituted, are substituted with a substituent subjected to a nucleophilic substitution fluorination reaction; and an organic compound wherein one or two or more hydrogen atoms on an optionally substituted aromatic compound are substituted with a substituent subjected to a nucleophilic substitution fluorination reaction. They are converted to the corresponding organic compound wherein one or two or more hydrogen atoms on a saturated hydrocarbon, which may be substituted, are substituted with a fluorine atom; and an organic compound wherein one or two or more hydrogen atoms on an optionally substituted aromatic compound are substituted with a fluorine atom, respectively.

[0019]

Examples of the saturated hydrocarbon include a straight chain, branched chain or cyclic C1-C20 alkane such as methane, ethane, propane, n-butane, isobutane, n-pentane, n-decane, cyclopropane, 2,2-dimethylcyclopropane, cyclopentane and cyclohexane. The saturated hydrocarbon may be substituted with an optionally substituted C5-C20 aryl group such as a phenyl group, a 1-naphthyl group, a 2-naphthyl group, a 4-methylphenyl group, a 4-methoxyphenyl group, a 3-phenoxyphenyl group, a 2,3,5,6-tetrafluorophenyl group, a 2,3,5,6-tetrafluoro-4-methylphenyl group, a 2,3,5,6-tetrafluoro-4-methoxyphenyl group, a 2,3,5,6-tetrafluoro-4-methoxymethylphenyl group and a 2-pyridyl group; an optionally substituted C1-C20 alkoxy group such as a methoxy

group, an ethoxy group, an n-propoxy group, an isopropoxy group, an n-butoxy group, an isobutoxy group, a sec-butoxy group, a tert-butoxy group and a trifluoromethoxy group; an optionally substituted C6-C20 aryloxy group such as a phenoxy group, a 2-methylphenoxy group, 4-methylphenoxy group, 4-methoxyphenoxy group and 3-phenoxyphenoxy group; an optionally substituted C7-C20 aralkyloxy group such as a benzyloxy group, a 4-methylbenzyloxy group, a 4-methoxybenzyloxy group, a 3-phenoxybenzyloxy group, a 2,3,5,6-tetrafluorobenzyloxy group, a 2,3,5,6-tetrafluoro-4-methylbenzyloxy group, a 2,3,5,6-tetrafluoro-4-methoxybenzyloxy group and a 2,3,5,6-tetrafluoro-4-methoxymethylbenzyloxy group; a fluorine atom; an optionally substituted C2-C20 alkylcarbonyl group such as an acetyl group and an ethylcarbonyl group; an optionally substituted C7-C20 arylcarbonyl group such as a benzoyl group, a 2-methylbenzoyl group, a 4-methylbenzoyl group and a 4-methoxybenzoyl group; an optionally substituted C8-C20 aralkylcarbonyl group such as a benzylcarbonyl group, a 4-methylbenzylcarbonyl group and a 4-methoxybenzylcarbonyl group; a carboxyl group; or the like. Examples of the saturated hydrocarbon which is substituted with the substituent include fluoromethane, trifluoromethane, methoxymethane, ethoxymethane, methoxyethane, toluene, 4-methoxytoluene, 3-phenoxytoluene, 2,3,5,6-tetrafluorotoluene, 2,3,5,6-tetrafluoro-paraxylene, 2,3,5,6-tetrafluoro-4-methoxytoluene, 2,3,5,6-tetrafluoro-4-methoxymethyltoluene, 2-propylnaphthalene, methyl isobutyl ketone, acetophenone, 4-methylacetophenone and phenylacetone.

[0020]

Examples of the aromatic compound include a hydrocarbon type aromatic compound such as benzene and naphthalene, and a heteroaromatic compound such as pyridine and quinoline. The aromatic compound may be substituted with an optionally substituted C<sub>5</sub>-C<sub>20</sub> aryl group such as a phenyl group, a 1-naphthyl group, a 2-naphthyl group, a 4-methylphenyl group, a 4-methoxyphenyl group, a 3-phenoxyphenyl group, a 2,3,5,6-tetrafluorophenyl group, a 2,3,5,6-tetrafluoro-4-methylphenyl group, a 2,3,5,6-tetrafluoro-4-methoxyphenyl group, a 2,3,5,6-tetrafluoro-4-methoxymethylphenyl group and a 2-pyridyl group; an optionally substituted C<sub>1</sub>-C<sub>20</sub> alkoxy group such as a methoxy group, an ethoxy group, an n-propoxy group, an isopropoxy group, an n-butoxy group, an isobutoxy group, a sec-butoxy group, a tert-butoxy group and a trifluoromethoxy group; an optionally substituted C<sub>6</sub>-C<sub>20</sub> aryloxy group such as a phenoxy group, a 2-methylphenoxy group, 4-methylphenoxy group, 4-methoxyphenoxy group and 3-phenoxyphenoxy group; an optionally substituted C<sub>7</sub>-C<sub>20</sub> aralkyloxy group such as a benzyloxy group, a 4-methylbenzyloxy group, a 4-methoxybenzyloxy group, a 3-phenoxybenzyloxy group, a 2,3,5,6-tetrafluorobenzyloxy group, a 2,3,5,6-tetrafluoro-4-methylbenzyloxy group, a 2,3,5,6-tetrafluoro-4-methoxybenzyloxy group and a 2,3,5,6-tetrafluoro-4-methoxymethylbenzyloxy group; an optionally substituted C<sub>2</sub>-C<sub>20</sub> alkylcarbonyl group such as an acetyl group and an ethylcarbonyl group; an optionally substituted C<sub>7</sub>-C<sub>20</sub> arylcarbonyl group such as a benzoyl group, a 2-methylbenzoyl group, a 4-methylbenzoyl group and a 4-methoxybenzoyl group; an optionally substituted C<sub>8</sub>-C<sub>20</sub> aralkylcarbonyl group such as a benzylcarbonyl group, a 4-methylbenzylcarbonyl group and a 4-methoxybenzylcarbonyl



group; a carboxyl group; a sulfonamide group; a cyano group; an amide group; a fluorine atom; or the like. Alternatively, neighboring substituents among these substituents may be bonded each other to form a ring together with carbon atoms to which they are bonded. Among substituents which the aromatic compound may have, an electron withdrawing substituent is preferable in terms of the reactivity. Examples of the electron withdrawing substituent include a fluorine atom, an optionally substituted alkylcarbonyl group, an optionally substituted aralkylcarbonyl group, an optionally substituted arylcarbonyl group, a carboxyl group, a sulfonamide group and a cyano group. Examples of the aromatic compound substituted with the substituent include cyanobenzene, terephthalonitrile, isophthalonitrile, orthophthalonitrile, fluorobenzene, 1,4-difluorobenzene, benzenesulfonamide, biphenyl, 2-phenylnaphthalene, diphenyl ether, 3-methylpyridine, 4-phenylpyridine, benzophenone and 1,2-diphenylethanone.

[0021]

Examples of the substituent subjected to a nucleophilic substitution fluorination reaction, which is substituted with a hydrogen atom on the saturated hydrocarbon or the aromatic compound, include a chlorine atom, a bromine atom, an iodine atom, a nitro group, a sulfo group, an optionally substituted alkylsulfonyloxy group, an optionally substituted arylsulfonyloxy group, an optionally substituted alkylcarbonyloxy group and an optionally substituted arylcarbonyloxy group. In the case of having two or more substituents, these may be same or different from each other.

[0022]

Examples of the optionally substituted alkylsulfonyloxy group include a methanesulfonyloxy group, an ethanesulfonyloxy group and

a trifluoromethanesulfonyloxy group. Examples of the optionally substituted arylsulfonyloxy group include a paratoluenesulfonyloxy group, a benzenesulfonyloxy group and a 1-naphthalenesulfonyloxy group. Examples of the optionally substituted alkylcarbonyloxy group include a trifluoroacetoxy group and a pentafluoroethylcarbonyloxy group. Examples of the optionally substituted arylcarbonyloxy group include a tetrafluorobenzoyloxy group and a benzoyloxy group.

[0023]

Examples of the organic compound having one or two or more substituents subjected to a nucleophilic substitution fluorination reaction include 1-chlorobutane, 1-bromobutane, 1-iodobutane, 1-chlorocyclobutane, 1-chloropentane, 1-bromopentane, 1-chlorocyclopentane, 1-chloro-4-bromobutane, 1-chlorohexane, 1-bromohexane, 1,6-dibromohexane, 1-chloroheptane, 1-bromoheptane, 1-chlorooctane, 1-bromooctane, benzyl chloride, benzyl bromide, 4-methoxybenzyl chloride, 4-methylbenzyl bromide, 3,4,5-trifluorobenzyl bromide, n-butyl paratoluenesulfonate, n-butyl methanesulfonate, n-pentyl paratoluenesulfonate, n-pentyl methanesulfonate, n-hexyl paratoluenesulfonate, n-hexyl methanesulfonate, n-heptyl paratoluenesulfonate, n-heptyl methanesulfonate, n-octyl paratoluenesulfonate, n-octyl methanesulfonate, n-butyl trifluoroacetate, n-butyl tetrafluorobenzoate, n-octyl trifluoroacetate, 4-chloronitrobenzene, 4-bromonitrobenzene, 2-chloronitrobenzene, 2-bromonitrobenzene, 4-cyanochlorobenzene, 4-cyanobromobenzene, 1-chloro-2,4-dinitrobenzene, tetrachloroterephthalonitrile, tetrachloroisophthalonitrile, tetrachloroorthophthalonitrile, 1,3-dichloro-4,6-dinitrobenzene, 2-chloroquinoline,

2-chloro-5-nitropyridine and 2-chloro-5-trifluoromethylpyridine.

[0024]

In the present invention, a fluorine-containing compound can be obtained by reacting the organic compound having one or two or more substituents subjected to a nucleophilic substitution fluorination reaction with the fluorinating agent (1). Herein, when the organic compound having two or more substituents subjected to a nucleophilic substitution fluorination reaction is used, those may be different substituents and the reactivity is usually shown as following; only the highest reactive substituent is sometimes substituted with a fluorine atom and same or different two or more substituents are sometimes substituted with fluorine atoms.

[0025]

In the reaction of the organic compound wherein one or two or more hydrogen atoms on an optionally substituted aromatic compound are substituted with the substituent subjected to a nucleophilic substitution fluorination reaction, when the optionally substituted aromatic compound is the hydrocarbon type aromatic compound, the substituent subjected to a nucleophilic substitution fluorination reaction, which has an electron-withdrawing group on para- or ortho-position, is usually preferentially substituted with a fluorine atom. For example, in the reaction of 4-chloronitrobenzene, although both of the chlorine atom and the nitro group are substituents subjected to a nucleophilic substitution fluorination reaction, the chlorine atom having higher electron-withdrawing nitro group on para-position is preferentially substituted with a fluorine atom and 4-fluoronitrobenzene is usually selectively produced. Of course, the nitro group can be also substituted with a fluorine atom by selecting accordingly reaction conditions such as use of a large excess of

the fluorinating agent (1), and paradifluorobenzene can be also obtained.

[0026]

Alternatively, in the reaction of the organic compound wherein one or two or more hydrogen atoms on an optionally substituted aromatic compound are substituted with the substituent subjected to a nucleophilic substitution fluorination reaction, when the optionally substituted aromatic compound is the heteroaromatic compound, the substituent subjected to a nucleophilic substitution fluorination reaction on the 2-, 4- or 6-position for the heteroatom constituting the heteroaromatic ring, is usually preferentially substituted with a fluorine atom. For example, in the case of 2-chloro-3-nitropyridine, the chlorine atom on 2-position is usually substituted to yield 2-fluoro-3-nitropyridine. Off course, the nitro group can be also substituted with a fluorine atom by selecting accordingly reaction conditions such as use of a large excess of the fluorinating agent (1), and 2,3-difluoropyridine can be also obtained.

[0027]

The used amount of the fluorinating agent (1) is usually 1 mole or more per 1 mole of the substituent desired to substitute with a fluorine atom on the organic compound having one or two or more substituents subjected to a nucleophilic substitution fluorination reaction. While there is no upper limit particularly, when the compound has only one substituent subjected to a nucleophilic substitution fluorination reaction, it is preferably in a range of about 1.5 to 5.0 moles per 1 mole of the substituent subjected to a nucleophilic substitution fluorination reaction from the viewpoint of the reaction efficiency. Alternatively, when the compound has two or more substituents subjected to a nucleophilic substitution

fluorination reaction, the used amount thereof may be accordingly set in a range wherein the substituent, which is not desired to subject to the fluorination reaction, is not substituted with a fluorine atom based on the above-mentioned priority of the reactivity.

[0028]

The present invention can be carried out in the presence of an organic solvent, water or a mixture thereof, and can be also carried out in the absence of the solvent.

[0029]

Examples of the organic solvents in the case of being carried out using the solvent include ether solvents such as methyl tert-butyl ether and tetrahydrofuran; nitrile solvents such as acetonitrile and propionitrile; aromatic hydrocarbon solvents such as toluene and xylene; aliphatic hydrocarbon solvents such as cyclohexane and n-heptane; amide solvents such as dimethylformamide and dimethylacetamide; and sulfur-containing solvents such as sulfolane and dimethylsulfoxide.

[0030]

When the solvent is used, the used amount thereof is not particularly limited, and it is practically about 100 parts by weight or less per 1 part by weight of the fluorinating agent (1) in consideration of volumetric efficiency.

[0031]

When the reaction temperature is too low, the reaction hardly proceeds and, when the reaction temperature is too high, side reaction such as degradation of the starting material or product may proceed. Therefore, the practical reaction temperature is usually a range of about -20 to 200°C.

[0032]

The mixing order of the reaction agents is not particularly limited. For example, the fluorinating agent (1) may be added to the organic compound having one or two or more substituents subjected to a nucleophilic substitution fluorination reaction under the reaction temperature condition and the reaction may be carried out in the reverse order. Alternatively, the reaction temperature may be adjusted after mixing both agents simultaneously.

[0033]

The present reaction may be carried out at normal pressure and under pressure. Alternatively, the progress of the reaction can be checked by a conventional analytical means such as gas chromatography, high performance liquid chromatography, thin layer chromatography, NMR and IR.

[0034]

After completion of the reaction, the fluorine-containing compound which is the reaction product can be isolated by conducting crystallization treatment, distillation or concentration of the organic layer obtained by extracting, if necessary by adding water and/or a water-insoluble solvent thereto. The fluorine-containing compound isolated may be further purified by a means such as distillation or column chromatography.

[0035]

Herein, examples of the water-insoluble solvents include aromatic hydrocarbon solvents such as toluene, xylene and chlorobenzene; aliphatic hydrocarbon solvents such as pentane, hexane and heptane; halogenated hydrocarbon solvents such as dichloromethane, dichloroethane and chloroform; ether solvents such as diethyl ether, methyl tert-butyl ether and tetrahydrofuran; and ester solvents such as ethyl acetate.

[0036]

Examples of the fluorine-containing compound thus obtained include 1-fluorobutane, 1-fluorocyclobutane, 1-fluoropentane, 1-fluorocyclopentane, 1,4-difluorobutane, 1-chloro-4-fluorobutane, 1-fluorohexane, 1,6-difluorohexane, 1-fluoroheptane, 1-fluorooctane, benzyl fluoride, 4-methoxybenzyl fluoride, 4-methylbenzyl fluoride, 3,4,5-trifluorobenzyl fluoride, 4-fluoronitrobenzene, 2-fluoronitrobenzene, 4-cyanofluorobenzene, 1-fluoro-2,4-dinitrobenzene, tetrafluoroterephthalonitrile, tetrafluoroisophthalonitrile, tetrafluoroorthophthalonitrile, 1,3-difluoro-4,6-dinitrobenzene, 2-fluoroquinoline, 2-fluoro-5-nitropyridine and 2-fluoro-5-trifluoromethylpyridine.

[0037]

After the reaction, the alkyl-substituted imidazolium cation can be recovered as the mixed alkyl-substituted imidazolium salt containing the substituent subjected to a nucleophilic substitution fluorination reaction. The mixed alkyl-substituted imidazolium salt recovered by filtration treatment or separation treatment from the reaction liquid, can be reused as the fluorinating agent (1) by exchanging to fluoride ion again.

[Example]

[0038]

The present invention will be further illustrated in more detail by Examples. The present invention is not limited to these Examples.

[0039]

Experiment 1 (Example of synthesis of the fluorinating agent (1))

Into an Erlenmeyer flask, 5.0 g of 1-methyl-3-(n-butyl)imidazolium chloride and 50 g of water were

charged and dissolved. After 1.72 g of silver(I) fluoride and 30 g of water were charged into another Erlenmeyer flask to be dissolved, two aqueous solutions were mixed at 25°C and the stirring was continued for 30 minutes at the same temperature. The crystalline precipitated after the reaction was filtered and washed with water. The filtrate and wash liquid obtained were joined and concentrated to obtain 5.8 g of the colorless oil. This oil was liquid even at 0°C. The obtained oil was identified as the dihydrate of the salt consisting of the mixed anion consisting of 47.5 mol% of the fluoride ion and 52.5 mol% of the chloride ion, and the 1-methyl-3-n-butylimidazolium cation from the result of elementary analysis.

Yield: 100%.

[0040]

Elementary analytical value: C: 48.2, H: 9.5, N: 14.1, F: 4.6, Cl: 9.5

Calculated value: C: 47.4, H: 9.5, N: 13.8, F: 4.5, Cl: 9.2

<sup>1</sup>H-NMR (δ ppm, DMSO-d<sub>6</sub>, TMS standard): 0.88 (t, 3H), 1.25 (m, 2H), 1.78 (m, 2H), 3.90 (s, 3H), 4.19 (t, 2H), 7.85 (d, 2H), 10.0 (bs, 1H)

[0041]

Experiment 2 (Example of synthesis of the fluorinating agent (1))

Into an Erlenmeyer flask, 5.0 g of 1-methyl-3-(n-butyl)imidazolium chloride and 50 g of water were charged and dissolved. After 3.0 g of silver(I) fluoride and 30 g of water were charged into another Erlenmeyer flask and dissolved, two aqueous solutions were mixed at 25°C and the stirring was continued for 30 minutes at the same temperature. The crystalline precipitated after the reaction was filtered and washed with water. The filtrate and wash liquid obtained were joined and concentrated to obtain 5.6



g of the colorless oil. A part of this oil crystallized at room temperature. The obtained oil was identified as the dihydrate of the salt consisting of the mixed anion consisting of 83 mol% of the fluoride ion and 17 mol% of the chloride ion, and the 1-methyl-3-n-butylimidazolium cation from the result of elementary analysis.

Yield: 99%.

[0042]

Elementary analytical value: C: 47.3, H: 9.8, N: 13.8, F: 8.1, Cl: 3.1

Calculated value: C: 48.7, H: 9.7, N: 14.2, F: 8.0, Cl: 3.1

<sup>1</sup>H-NMR ( $\delta$  ppm, DMSO-d<sub>6</sub>, TMS standard): 0.88 (t, 3H), 1.20 (m, 2H), 1.75 (m, 2H), 3.88 (s, 3H), 4.19 (t, 2H), 7.85 (d, 2H), 9.85 (s, 1H)

[0043]

#### Example 1

Into a 50 mL flask equipped with a reflux condenser, 640 mg of the fluorinating agent (1) synthesized in Experiment 1 and 254 mg of benzyl chloride were charged and the resulting mixture was stirred for 3 hours at 80°C. After cooling to room temperature, 5 g of ethyl acetate was added thereto and stirred. The mixture was separated to two layers by standing. The upper layer was analyzed by gas chromatography (internal standard method) to find out that the main product was benzyl fluoride.

Yield: 75% (based on benzyl chloride). Benzyl chloride was recovered in 25%.

Yield based on the fluoride ion of the fluorinating agent (1) was 100%.

[0044]

#### Example 2

Into a 50 mL flask equipped with a reflux condenser, 300 mg of the fluorinating agent (1) synthesized in Experiment 2, 127 mg of benzyl chloride and 500 mg of acetonitrile were charged and the resulting mixture was stirred for 3 hours at 80°C. After cooling to room temperature, 5 g of ethyl acetate was added thereto and stirred. The mixture was separated to two layers by standing. The upper layer was analyzed by gas chromatography (internal standard method) to find that the main product was benzyl fluoride.

Yield: 99% (based on benzyl chloride). Benzyl chloride was recovered in 1%.

Yield based on the fluoride ion of the fluorinating agent (1) was 79%.

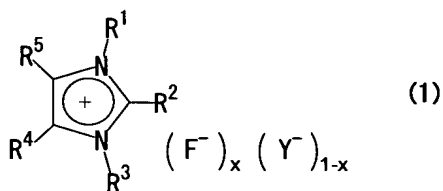
[Title of Document] ABSTRACT

[Abstract]

[Problem] It is to provide an industrially advantageous method for producing a fluorine-containing compound.

[Means to Solve] A method for producing a fluorine-containing compound comprising reacting an organic compound having one or two or more substituents subjected to a nucleophilic substitution fluorination reaction with a mixed alkyl-substituted imidazolium salt containing a fluoride ion represented by the formula (1):

[Formula 1]



wherein  $R^1$  and  $R^3$  are the same or different, and each represents an optionally substituted alkyl group,  $R^2$ ,  $R^4$  and  $R^5$  are the same or different, and each represents a hydrogen atom or an optionally substituted alkyl group,  $Y^-$  represents a monovalent anion other than a fluoride ion, and  $0 < x < 1$ .

[Selected Figure] None

### Applicant History Information

Identification No.: [000002093]

1. Changing Date: August 28, 1990

[Reason for changing] Newly registration

Address: 5-33, Kitahama 4-Chome, Chuo-ku,  
Osaka-shi, Osaka-fu

Name: Sumitomo Chemical Company, Limited

2. Changing Date: October 1, 2004

[Reason for changing] Name changing

Address changing

Address: 27-1, Shinkawa 2-Chome, Chuo-ku, Tokyo

Name: Sumitomo Chemical Company, Limited